Research Progress of Intestinal Flora and Functional Constipation

Liangwu Huang¹, Hua Jiang²,*, Zongrun Li¹, Wenxin Li¹

¹Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China.
²The Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China.

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*Corresponding author: Hua Jiang, The Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China. Email: jhsd2004@163.com

Abstract

Functional constipation is a common gastrointestinal functional disease in clinical practice. It is mainly manifested in less stool volume, reduction of defecation times, extension of defecation space, hardness of feces and difficulty in defecation. It will cause mental disorders to patients and seriously affect people’s quality of life. Long term functional constipation will not only affect people’s quality of life and mental health, but also lead to common anorectal diseases such as hemorrhoids and anal fissure. In severe cases, it will affect the cardiovascular and cerebrovascular system of the elderly. In recent years, studies have found that intestinal flora imbalance, as one of the main pathogenic factors of FC, plays an important role in the pathogenesis of FC. Therefore, it is of great significance to correct the flora disorder for the treatment of functional constipation. Therefore, this article takes the intestinal flora as the target, and expounds the research progress of intestinal flora and functional constipation from four aspects: probiotics, prebiotics, synbiotics and fecal bacteria transplantation.

Keywords

Functional Constipation, Disturbance of Intestinal Flora, Microbial Preparations, Fecal Bacteria Transplantation

Functional constipation (FC) is caused by non intestinal diseases, systemic organic diseases or drugs. It is a common gastrointestinal functional disease in clinic [1]. The disease is more common in young children and the elderly. Its clinical manifestations are less stool volume, less defecation times, longer defecation space, hardness of feces and difficulty in defecation. Long term functional constipation will not only affect people’s quality of life and mental health, but also lead to common anorectal diseases such as hemorrhoids and anal fissure. In severe cases, it will affect the cardiovascular and cerebrovascular system of the elderly. At present, in FC treatment, western medicine mostly focuses on various laxatives and gastric motility promoting drugs, but the treatment effect is poor [2, 3]. Long term use of laxatives will not only make patients dependent, but also may produce other side effects, such as intestinal melanosis, rectal prolapse, etc. In traditional Chinese medicine treatment, traditional Chinese medicine decoction, acupoint application, moxibustion and acupuncture are used together, especially traditional Chinese medicine decoction has a significant effect in the treatment of FC. In recent years, studies have found that the imbalance of intestinal flora can lead to the occurrence of FC, and there are certain differences in intestinal flora between FC patients and healthy people. Therefore, correcting the imbalance of intestinal flora is of great significance for the treatment of FC.

1. Etiology and pathogenesis of functional constipation

Western medicine believes that the causes of FC are multifaceted. At present, studies have found that FC is
mainly related to factors such as the imbalance of intestinal flora, the abnormality of Cajal interstitial cells, the disorder of nervous system, lack of bowel movement and so on [4]. According to their clinical symptoms, they can be divided into slow transit constipation (STC), outlet obstructive constipation (OOC) and mixed constipation (MC) [5, 6]. STC is mainly caused by the weakening of the peristalsis ability of the large intestine due to various reasons, which prolongs the existence time of feces in the whole gastrointestinal tract or colon, mainly manifested as abdominal pain, abdominal distension, reduction of the number of defecation, dry feces, and less stool intention. OOC refers to constipation caused by abnormal muscles near the pelvis, such as rectocele, pelvic floor Achalasia Syndrome, perineum descent syndrome, etc. It is characterized by laborious defecation, unconstrained defecation, pain in the anus, and sometimes need to assist with defecation by hand. Defecography can assist in diagnosis. MC has the clinical characteristics of both constipations. The two can cause and affect each other and transform each other. Most of them belong to intractable constipation [7].

Chinese medicine believes that although constipation occurs in the large intestine, it is closely related to the five viscera, diet and emotions. Its etiology is multifaceted, mainly including exogenous evil, deficiency of Qi, blood, yin and Yang, emotional stimulation and careless diet. If the function of the lung tongtiao channel is lost, and the body fluid cannot flow down to the large intestine, it will lead to dry stool. In addition, if the lung fluid is insufficient, the fluid injury will turn into dryness, and the lung and large intestine are in and out of each other. If the lung fluid dryness passes down to the large intestine, it will also lead to the dryness of the stool. The liver governs catharsis. If the liver is injured due to emotional depression or anger, it will lead to stagnation of liver qi, blocked Qi mechanism and blocked Fu Qi. The spleen governs the movement and transformation, and the deficiency of Spleen Qi will lead to the dysfunction of the movement and transformation function, further leading to the loss of the conduction function of the large intestine and the stagnation of the stool in the intestines. The kidney governs the water and governs the two stools. If the kidney Yin is insufficient, it cannot control the Yang, and the deficiency fire will lead to the internal knot of the stool. Kidney yang deficiency cannot warm the large intestine, and the loss of large intestine conduction function will make the stool stagnate in the intestine. In addition, anorectal diseases such as anal fissure and hemorrhoids, or anorectal diseases after operation due to pain or poor defecation, make patients fear defecation, which makes feces stay in the intestine, and can also lead to constipation. In addition, the above etiology and pathogenesis can also be transformed into each other or both. For example, Qi block turns into heat for a long time, heat knot for a long time, consumes fluid and injures body fluid, and can lead to yin deficiency. In short, constipation takes deficiency and excess as the key link. Deficiency and excess can be transformed into each other, from deficiency to excess, from excess to deficiency, and from deficiency to excess. According to the different causes and pathogenesis of constipation, constipation can be divided into solid secret and empty secret. Solid secret includes Qi secret (Liumo Decoction), heat secret (maziren pill) and cold secret (Wenpi Decoction). Deficiency secret can be divided into Qi deficiency secret (Huangqi Decoction), blood deficiency secret (Runchang pill), yin deficiency secret (Zengye Decoction) and yang deficiency secret (Jichuan Decoction).

2. Intestinal flora

Human gastrointestinal tract is inhabited by thousands of microorganisms with a total number of 1014. These microorganisms include bacteria, fungi, protozoa, etc., which together constitute the human intestinal microbiology [8]. According to their different effects on human body, they can be divided into three categories: beneficial bacteria, harmful bacteria and neutral bacteria. Beneficial bacteria refer to the bacteria that have a positive effect on the human body, which can promote the peristalsis of the gastrointestinal tract, help the digestion of food, and synthesize various vitamins beneficial to the human body, mainly including bifidobacteria and lactic acid bacteria. Harmful bacteria will have a negative impact on the human body, leading to the occurrence of various diseases. They are potential risk factors leading to gastrointestinal tumors, such as Bacillus aeruginosa, Bacillus typhi, etc. Neutral bacteria are located between the two. In general, they do not produce any positive and negative effects. They mainly produce positive effects in healthy people. However, under the influence of other factors, once they proliferate or transfer to other parts of the human body, they will produce various negative effects, leading to the occurrence of diseases. In a healthy human body, these intestinal microflora are in a balanced state, but when the intake of food, human factors or bacterial factors change, the beneficial bacteria decrease and the harmful bacteria increase, this balance will be broken, and the human body will have a variety of symptoms [9, 10]. According to the research [11, 12, 13, 14, 15, 16], compared with normal people, the intestinal flora of FC patients is mainly manifested in the decrease of anaerobic bacteria represented by bifidobacteria and lactobacilli and the increase of pathogenic bacteria represented by aeruginosa and Clostridium putrefaciens. At present, the research mechanism of regulating intestinal flora to treat FC is not clear. At present, there are mainly the following conjectures [17]: 1) bac-
terial fermentation or fermentation end products; 2) Intestinal neuroendocrine factors; 3) Mediators released by the intestinal immune response.

3. Microecological treatment of FC

At present, FC is mainly treated with various laxatives, but its therapeutic effect is poor and there are many side effects. Microecological agents have less adverse reactions. They can maintain the flora balance of the gastrointestinal tract by improving the gastrointestinal flora environment in FC patients, promoting the production of beneficial bacteria and inhibiting harmful bacteria. They can be used as the first choice for long-term adjuvant medication of FC [18]. At present, the clinical applications mainly include probiotics, prebiotics and synbiotics [19]. In addition, faecal microbiota transplantation (FMT) also belongs to the broad intestinal microecological therapy.

3.1 Probiotics

Probiotics refer to a kind of microorganisms beneficial to human body, which are mainly colonized in human gastrointestinal tract. They can produce beneficial effects by regulating the balance of intestinal flora or inhibiting pathogenic bacteria, and have high stability and no side effects. Hushuangli and liuyuntao [20] found that the effective rate of probiotics combined with procarbil succinate was higher than that of the comparison group through the study of 204 FC patients. In addition, the adverse reactions were lower than that of the comparison group, and the recurrence rate after 6 months was also lower than that of the comparison group. Pengrujie and Zeng Qingxin [21] found that probiotics combined with lactulose had better effect in improving constipation symptoms and psychological status of elderly patients through the study of 206 elderly FC patients. Qian min et al. [22] found that on the basis of the control group, the combined use of Peifeikang and Miya probiotics improved the defecation cycle, Wexner score and stool properties significantly compared with those before the treatment, with fewer adverse reactions. It is better than the use of lactulose alone in improving intestinal microecology and restoring intestinal function.

3.2 Prebiotics

Prebiotics refer to some organic substances that are not absorbed by the human body but can selectively promote the metabolism and proliferation of beneficial bacteria in the body. Common prebiotics include lactulose, inulin, xylo oligosaccharides, etc. [23]. In addition, water-soluble fiber and insoluble fiber also belong to the category of prebiotics. Water soluble fiber can increase the moisture in feces and increase its wetness; Insoluble fibers increase fecal volume and stimulate colonic peristalsis [24]. Zhongjingye et al. [25] found that on the basis of the control group, the combination of lactulose in the treatment of elderly refractory FC can promote gastrointestinal peristalsis, improve constipation symptoms and reduce the recurrence rate. Lei Yanwei et al. [26] found that the total effective rate of treatment with lactulose solution was 85.0% and the side effects were less through the study of 120 FC children.

3.3 Synbiotics

Synbiotics are probiotics composed of prebiotics and probiotics. Huang Linsheng and others [27] found that the constipation symptoms of the patients were significantly relieved after synbiotic treatment, and the intestinal flora was significantly changed at the genus level compared with that before treatment. Jinqingchong et al. [28] studied 93 FC patients and concluded that heshengyuan preparation can improve intestinal flora disorder, promote gastrointestinal peristalsis and alleviate clinical symptoms.

3.4 FMT treatment

FMT refers to the transplantation of functional flora in the feces of healthy people into the intestines of patients through various ways to rebuild new intestinal flora, so as to achieve the treatment of diseases [28]. There are thousands of intestinal microflora in the human gastrointestinal tract. However, the current clinical microbial preparations are relatively single, which can not completely restore the balance of the intestinal microflora. However, nearly 100 microorganisms are contained in every 1g of feces of healthy people. Therefore, FMT treatment is of great significance in restoring the gastrointestinal microflora. Gehong’s “urgent prescription for elbow reserve” states that “one liter of fecal juice makes you live”. This is the earliest record that feces are widely recognized in China to treat human diseases. It is also recorded in the human part of compendium of Materia Medica written by lishizhen in the Ming Dynasty that human feces are used to treat various diseases. However, in the world, FMT was first proposed by Eiseman et al. in 1958. It is mainly used to treat pseudomembranous enteritis, but its operation
method is relatively simple. It is mainly enema with fecal solution of healthy people. The modern standardized FMT in China began in 2012, which was first carried out and popularized by Professor Zhang Fanfa, and is mainly applied to Clostridium difficile infection, ulcerative colitis and other diseases. FMT was first used to treat FC in 1989. It was started by body [29], and the curative effect is relatively significant with few side effects. At present, FMT is administered through the upper digestive tract, the middle digestive tract and the lower digestive tract. The upper digestive tract is mainly administered by enema. However, enema is difficult to administer to the whole intestinal tract, and drugs cannot exist in the intestinal tract for a long time. In terms of donor selection, it is divided into autologous and allogeneic. At present, allogeneic is the main type, mainly young college students or relatives who are healthy, have not used antibiotics within three months, have no gastrointestinal diseases, and have no infectious diseases. The adverse reactions of FMT treatment are less. Even if they exist, they are mostly mild gastrointestinal symptoms, and most of them are caused by their primary diseases [30]. At present, FMT treatment is rarely used in China, and is less used to treat FC. There is little clinical evidence, and there is a lack of supporting data. A foreign report shows that 2 patients treated with FMT have serious bacterial infection, and the bacteria come from the feces provided by the donor. Therefore, careful selection and application should be made on whether to select patients for FMT treatment, the selection of donors, and the preparation and preservation of fecal bacterial suspension to reduce the occurrence of adverse reactions [31].

4. Summary

At present, the pathogenesis of FC is not clear. Therefore, in terms of treatment, it is necessary to clarify its systemic and local causes and carry out etiological treatment. Therefore, while giving the necessary drug treatment, we must correct the bad living habits, improve the diet structure, increase the amount of activity, and carry out surgical treatment when necessary. However, the long-term use of microbiological agents may lead to the disorder of intestinal flora again. Therefore, the use of microbiological agents should be under the guidance of doctors. It is not allowed to use drugs blindly. Moreover, the drugs are mainly used in combination, and the drugs used alone are less. As one of the new methods to treat FC, FMT has less adverse reactions and good therapeutic effect. It is a highly recommended treatment method at present. However, the research basis of this method is not sufficient, there are few clinical trials, and there is insufficient evidence in the treatment of FC. Therefore, it is necessary to carefully select and apply FMT in the selection of patients, the selection of donors, and the preparation and preservation of fecal bacteria suspension. At present, the relevant national laws and regulations on FMT are relatively imperfect. Fortunately, FMT has not been fully promoted in China. To further promote FMT, relevant laws and regulations must be improved to ensure the safety and efficacy of fecal suspension or fecal bacteria capsule. In addition, the culture of traditional Chinese medicine is broad and profound. In the Yellow Emperor’s Internal Classic, there is a mention of diseases such as difficult defecation. Since then, various medical books have made a detailed elaboration on the etiology and pathogenesis of constipation, and the precise prescriptions for treating constipation are countless. TCM treats constipation as a whole, which can not only change the symptoms of constipation, but also improve the overall physical condition of the human body. Therefore, in the future research and clinical practice, we can further combine the dialectical treatment of traditional Chinese medicine, holistic medication and the regulation of intestinal flora, so as to achieve better curative effect, reduce patients’ pain and improve patients’ quality of life. The number of intestinal flora in human body is large and the types are complex. At present, most clinical studies are on the treatment of FC with a single flora. Therefore, in the future, we should increase the research on different microorganisms to further explore the mechanism of FC treatment.

References


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